In conclusion, rheumatoid arthritis if taken early and given adequate treatment will often subside and in many cases can be entirely eliminated. The present system of treatment is sound and it is doubtful if there will be any great change in it in the next ten years. Gold alone is not a cure for rheumatoid arthritis but gold along with modern treatment in a sanatorium including rest, heat, physiotherapy and psychotherapy gives a result which may well be called a cure. There may be recurrences later but this is also true of tuberculosis, pneumonia and the common cold.

If we are to stand by until the governments find a single cause or single cure for arthritis, many people with active rheumatoid arthritis now will be hopelessly crippled, when with adequate treatment they could be saved the pain and crippling. The entire program of the senior governments is to set aside a sum of money to try and find a cure for arthritis. This is a worthwhile project and may be a great boon to arthritics ten years from now but it neglects entirely today's active case. Clinical research is most important and to carry this out it is necesary to have large numbers of arthritics of all walks of life under treatment in adequate hospitals. This side of research is being sadly neglected.

REFERENCE

1. LUDWIG, SHORT AND BAUER: *New Eng. J. Med.*, **228**: 506, 1943.

RÉSUMÉ

L'auteur fait d'abord une description du processus évolutif de la maladie et de ses complications. L'étiologie est obscure mais la fatigue et les troubles moraux semblent avoir une influence assez marquée. Le diagnostic différentiel est assez facile et les seules difficultés proviennent d'une association de cette maladie avec d'autres lui ressemblant de près. En 1900 l'arthrite rhumatoïde était considérée comme incurable mais grâce aux nouvelles méthodes de diagnostic et de traitement les efforts sont maintenant plus souvent couronnés de succès et les statistiques grandement améliorées. Le premier traitement est le repos et la sédation. Les analyses d'usages sont compilées et un taux de sédimentation fait toutes les trois semaines. La physiothérapie est commencée dès le début. Le traitement à l'or est institué dès que le diagnostic est porté et continué pour 22 doses. Le plus fréquemment on emploie l'aspirine comme analgésique mais parfois des douleurs trop fortes nécessitent du démérol. L'alimentation doit être généreuse. Le taux de sédimentation n'est pas un indice sur de l'évolution de la maladie car il varie beaucoup, cependant dans l'ensemble il en donne une assez bonne idée. L'auteur insiste sur l'importance d'avoir des hôpitaux spécialisés pour ces patients et sur leur bas côut d'entretien. D'après son expérience personnelle avec les sels d'or il a trouvé qu "Lauron" était le moins toxique; il persiste encore 1% de troubles sérieux. Le BAL a été employé avec succès dans ces réactions. Les appareils plâtrés sont indiqués pour corriger les difformités. L'auteur conclut en appuyant sur l'efficacité actuelle des traitements. YVES PRÉVOST

A CLINICAL EVALUATION OF HYDRYLLIN AND TRIMETON (TRIPOTON) IN ALLERGIC MANIFESTATIONS*

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DURING the past year it was the writer's privilege to collaborate in the office investigation of two histamine antagonists, under the auspices of the Committee on Therapy of the American Academy of Allergy. The drugs were first submitted to the committee by the manufacturers, and screened by the committee's own pharmacologist as to potency and safety. If these requirements were met, ample supplies were sent to allergists in various parts of Canada and the United States for their clinical evaluation in their practices.

The first of these was "hydryllin",† a white tablet, consisting of 25 mgm. (3/8 gr.) diphenhydramine, the active base of diphenhydramine hydrochloride and 100 mgm. (1½ gr.) of aminophyllin. This combination was designed to produce the maximum effect of each, perhaps even to exert a synergist action. The addition of aminophyllin was for a twofold purpose, first to lessen the tendency for the familiar side reactions of the anti-histaminic, by its stimulating effect on the central nervous system, and secondly to widen its usefulness to include the asthmatics, by relaxing the bronchial muscles.

The second drug trimeton (tripoton)‡ was also a white tablet. Its chemical name is phenylpyridyl dimethyl propylamine or compound S 108. It was considered to be an anti-histaminic agent of high potency, but less toxic than other anti-histamines. In addition it was claimed that this particular compound has inherent anti-spasmodic properties.

For the purpose of this report and for the sake of brevity, the repetition of the detailed chemistry, formulæ, and pharmacologic action on animals is omitted. All this can be found in the literature supplied by the manufacturers. This report will be confined to my interpretation of the clinical results as found in private practice.

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† Supplied by Searle & Co., Chicago.

‡ Product of Schering Corporation, Bloomfield, N.J.

HYDRYLLIN

During the time hydryllin was used in the office the tablets were supplied to over 100 patients, usually as an adjunct to standard therapy. Of this group only 60 gave information of sufficient value for tabulation (see Table I). There were also about 35 patients who had already become acquainted with benadryl and/or pyribenzamine, and who experienced such profound unpleasant side reactions that they preferred not to take any "pills". These belonged chiefly to the "hay fever" group. It is appreciated that a proper statistical evaluation can not be made on reports from 60 patients, but only a clinical impression. The dosage varied from one or two tablets when necessary for attacks, to three times daily or at bedtime. Children were given ½ tablet with similar instructions. Some of them required and tolerated whole tablets. The ages of the patients ranged from 3 to 65 years. The time of onset of action of the drug varied from 15 minutes to 1 hour. The period of relief lasted from 2 hours to 12 hours.

Over 50% of the group taking hydryllin or 34 patients, were asthmatic (see Table I). Approximately 65% of the perennial asthmatics experienced varying degrees of relief from slight to good. About 75% of them reported no side effects. The toxic symptoms in order of frequency, were drowsiness, 20%, with weakness and headaches 5%. One case reported 100% relief but after several days the tablets seemed to lose their effect entirely. About 60% of the seasonal asthmatics with or without hay fever, reported relief, also varying from slight to good, with 25% having toxic reactions chiefly drowsiness 20%, with headache and weakness in a few instances. One patient in this group said her asthma was relieved but not her nasal symptoms. Incidentally she experienced sleepiness as a side reaction. One case of physical allergy got no relief but was made sleepy. The majority of those relieved could sleep better all night for which they were grateful. Basically the asthma was of course unaffected.

In regards to the seasonal allergic rhinitis cases of which there were 16 recorded (see Table I), 75% reported relief from "helpful" to good. Around 25% of this group complained of the usual toxic side effects. One patient felt worse generally and another received no relief after the second day. It might be noted that one patient waited 24 hours and when he got better anyway, did not take the pills given him. Finally with a small group of perennial allergic rhinitis (vasomotor rhinitis) cases, 75% reported relief from fair to very good. However about 30% had toxic effects. The majority of them were made sleepy: one complained of palpitation and another thought her symptoms were made worse. The several cases of urticaria referred for diagnostic study yielded disappointing results. Perhaps that was why they were referred, having previously used other antihistaminics to no avail.

To summarize, one may conclude that hydryllin is a satisfactory and safe anti-histaminic, producing a high percentage of relief in both the nasal and chest cases, particularly the former. This result was obtained as an adjunct to other therapy and its use was limited to a short period. The side effects, involving 1 in 4 were somewhat high.

TABLE I.

CLINICAL EFFECTS OF HYDRYLLIN

63	*Cases*	*Relief*	*Side effects* drowsiness	*No relief*
35	Perennial asthma	65%	25%	35%
	Seasonal asthma	60%	25%	40%
16	Hay fever	75%	25%	25%
12	Vasomotor rhinitis	75%	50%	25%

TRIMETON (TRIPOTON)

The investigation of trimeton followed that of hydryllin. Reasonably satisfactory information was received from 100 patients, divided between bronchial asthma, vasomotor rhinitis, seasonal hay fever and urticaria (see Table II). As with hydryllin it was adjuvant therapy in most cases. The dosage was one or two tablets, when needed or at bedtime, or one, three times daily. As a rule children were given ½ the adult dosage, although whole tablets were also taken without untoward effects. The ages of the patients ranged from 6 years to 62 years. The time of onset of action varied from 10 minutes to one hour. The period of relief lasted from 2 to 12 hours.

About 60% of the 24 cases of bronchial asthma experienced relief, mostly "good", with 10% complaining of either drowsiness or generalized weakness. As for the vasomotor rhinitis cases, of which there were 20, 75% reported relief from fair to excellent. In this group side effects occurred in about 20%. They experienced chiefly sleepiness, with head-

ache, dizziness or generalized weakness, in the minority.

The study was extended through the hay fever season, although the official experimental period expired June 30. There were 46 patients participating in the concomitant use of this drug, who were either pre-seasonally or co-seasonally treated with pollen extract injections. About 80% of them or 37 cases were satisfied with the temporary relief obtained, from fair to good. The relief, however, was not always maintained. The toxic effects reported in 10% of the cases were similar to those of the vasomotor rhinitis group. Ten cases of urticaria or angio-œdema, obtained only partial relief which was not consistent. One case of atopic eczema experienced no relief from the itching but did get headache, drowsiness and nausea.

To summarize, it would appear that trimeton (tripoton) is a safe and effective anti-histaminic agent with minimal side effects. In comparison with hydryllin, although similar percentages of asthmatic and hay fever patients were helped, the relief was better and the unpleasant side reactions involved a much smaller percentage. However in view of the relatively small number of cases recorded, this disparity might be more apparent than real.

TABLE II.
CLINICAL EFFECTS OF TRIMETON (TRIPOTON)

100	*Cases*	*Relief*	*Side effects*	*No relief*
24	Asthma	60%	drowsiness 10%	40%
20	Vasomotor rhinitis	75%	20%	25%
46	Hay fever	80%	10%	20%
10	Urticaria	70%	20%	30%

DISCUSSION

The list of histamine antagonists seems to be ever growing. Now physicians and self treaters have a wide choice of these drugs. The spontaneous remissions or self limiting nature of allergic symptoms are common knowledge. Along with a frequent underlying psychosomatic element one can expect a number of the patients to obtain some relief some of the time. Incidentally, the histamine theory of human allergy has not been fully established, nor generally accepted. It is probably only an important link in the chain of events culminating in the allergic symptoms. Early in the investigation it became apparent that reports from patients would tend to repetition so that a larger number of cases would not necessarily change the basic clinical value of the drugs under consideration. It is human nature to want to be most advanced and up-to-date. In practice we are all familiar with the urgent desire of many patients for a quick or painless "cure". As physicians, we may be tempted to supply this "magic" and so are apt to become prematurely over-enthusiastic about all these "wonder drugs", as well as to minimize any side reactions of a new therapeutic agent. Upon perusal of the voluminous literature on the subject reporting the apparent high degree of efficacy of the antihistaminics, with here and there a dissenting opinion, one is apt to get a wrong impression. Only when the observations on the individual patient are carried on for a much longer period than the tables indicate, does the true value of these drugs become apparent. It would then be discovered that many would report lack of consistency in obtaining relief, resulting in their discontinuing the medication. In retrospect, the interest in this revolutionary method of treatment must be similar to that which occurred with the advent of ephedrine. However I believe that in these antihistaminics we have a useful adjunct in our armamentarium. Something was needed besides ephedrine or epinephrine which are not always very effective or tolerated well. Furthermore, the antihistamine agents being palliative only, and not intended for continued use are not potent competitors with the established practice of proper allergic management. These words of conservatism are uttered with all due respect to the fine allergists who have published their clinical experiences and opinions on this subject.

CONCLUSION

Two histamine antagonists hydryllin and trimeton (tripoton), were investigated consecutively in a private practice. Almost all cases presenting themselves from day to day were given the drugs, unless refused from previous untoward experience with other antihistamines. These served as a separate panel of controls. In practically all cases it was adjuvant therapy. Both hydryllin and trimeton are apparently safe anti-histaminics giving a high percentage of temporary relief from the symptoms in varying degrees with unpleasant side effects in a small percentage. Hydryllin helped 60 to 65% of the asthmatic group, and

75% of the nasal cases. The chief side effect was drowsiness in 25 to 30%. With trimeton (tripoton), about 60% of the asthmatics were helped, and 75 to 80% of the nasal allergies were benefited, mostly with good to excellent effects, which was better than the results with hydryllin. The chief side effects of both agents were drowsiness occurring in 25 to 30% of the hydryllin cases, and 10 to 20% of the trimeton (tripoton) cases. These drugs although effective were palliative only, and in their long continued use the results became indifferent. Generally the urticarial patients were no better off with these drugs than the respiratory cases, and in my practice the results were disappointing. Finally anti-histaminic therapy should not replace standard allergic management.

The writer wishes to thank Dr. Chobot, Chairman of the Committee on Therapy, of the American Academy of Allergy, for the opportunity to do this work under official auspices.

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SUBMUCOUS LIPOMA OF THE COLON

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THE finding of neoplasms in the gastro-intestinal tract is a common incident in the practice of diagnostic roentgenology. Unfortunately the overwhelming majority of such tumours are malignant. This is particularly true of the colon, where frankly benign tumours are very uncommon. Among the benign lesions lipomas are second in frequency only to growths originating from the fibrous or muscular tissues of the intestinal wall. Lipomas may be submucous or subserous, the latter type being very rare and seldom clinically important. Several excellent reviews of the literature on submucous lipomas have appeared in recent years. Pemberton and McCormack reported a total of 116 cases in 1937, of which 97 were symptomatic clinical cases, and the remainder were incidental pathological discoveries. In 1946 Runyeon brought the list up to date with the addition of a further 21 cases from the literature plus 2 of his own. The present paper adds 7 cases gleaned from the literature since 1946, plus one new case reported herein. The cases reported by Moore in 1944 and Cabot in 1941 were evidently not included in Runyeon's summary and should also be added. This makes a grand total to date of 131 satisfactorily reported clinical cases.

TABLE I.

Runyeon, 1946	121 cases
Cabot, 1941	1 case (not included in above)
Moore, 1944	1 " (not included in above)
Schorr and Erlik, 1946	1 "
Gleize-Rambal and Paganelli, 1946	1 "
Threadgill, 1947	1 "
Pack and Booher, 1947	1 "
Mason and Linn, 1947	1 "
Spatolisano, 1947	1 "
Bradley, 1947	1 "

Obviously cases have been reported with accelerated frequency during recent years, suggesting that the condition is probably not so rare as the relatively small total of cases would suggest. Nevertheless, Threadgill states that only 6 intestinal lipomas were found in 44,654 intraperitoneal operations at the Mayo Clinic. Staemmler reported only 9 gastro-intestinal lipomas found in a series of 17,000 consecutive autopsies.

Etiology.—There is no satisfactory theory to account for the origin of lipomas. The favourite sites of occurrence in the colon are quite different to those of carcinoma. The common locations in the colon in order of frequency are: cæcum, ascending colon, sigmoid, transverse, rectum, and descending colon; 46% of the 121 cases analyzed by Runyeon occurred in the right colon. In relation to its length the incidence in the cæcum and ascending colon is 6 times that of the transverse and 4 times that of the left colon. They are definitely tumours of the cancer age, the average age in the 116 cases compiled by Pemberton and McCormack being 47.5 years. They are slightly commoner in females.

Pathology.—The tumour is composed of adult fat cells, surrounded by a capsule of connective tissue derived from the submucosa. As in superficial lipomas there may be a lobulated structure due to the presence of connective tissue septa. The base of the tumour may be quite vascular. The attachment to the bowel wall varies from a broad sessile type to a short pedicle. The surface of the tumour may be covered with intact intestinal epithelium, but, especially in the larger tumours, superficial ulceration is fairly common, and significant blood loss may result. Pedunculated growths

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